Applicants provisionally elect Group II, claims directed to methods for diagnosis of an arterial wall disruptive disorder by detecting a polypeptide marker indicative of macular degeneration. Applicants respectively traverse the restriction requirement. For example, the Office Action restricts Group II and Group III claims based on detection of a protein marker or a gene marker. Applicants respectfully note that any additional burden on the Examiner in considering the claims of Groups III and II together is not so serious because the two inventions are classified in the same class as indicated by the Examiner. In addition, the polynucleotide markers recited in Group III include those that encode protein markers recited in Group II. Therefore, Groups II and III are closed related and not necessarily patentable over each other. Applicants submit that considering Groups II and III together would not pose serious burden so as to require restriction, and withdrawal of the restriction requirements as between the claims of Group II and III is respectfully requested.

Similarly, Group VIII, IX and X are classified in the class and also the same subclass. Therefore, the restriction requirement is not proper under MPEP §808.02. Rather, if "the classification is the same and the field of search is the same and there is no clear indication of separate future classification and field of search, no reasons exist for dividing among related inventions." (MPEP 808.02; emphasis added). Since these groups are classified in the same class and subclass, searches of the two inventions would be coextensive. Therefore, as stated in MPEP §808.02, no reasons exist for dividing these inventions. Accordingly, Applicants respectfully request withdrawal of the restriction requirement as between the claims of Groups VIII, IX, and X.

Further, according to the Office Action, claims 1-10, 12, 14-20, 36, 37, and 67 are encompassed by Group II. However, Applicants note that claim 21 is also directed to detecting various protein markers (e.g., HLA-DR, CD68 and vitronectin). Claim 21 recites genotypic markers. It is to be noted a genotypic marker is not necessarily a gene marker (or a

polynucleotide marker). Rather, a genotypic marker can be a protein or a polypeptide, such as those recited in claim 21. Accordingly, claim 21 should be rejoined with Group II claims even if Groups II and III remain restricted.

Requirement for Election of Species

With respect to the Requirement for Election of Species, Applicants note that it is not clear from which species an election is required. The Office Action only stated that "Inventions II and III are directed to methods detecting different markers as claims 10, 13, 17, 18, 19, and 20 recite" and that "if invention II or II is elected, further election of a species is necessary." Claims 10, 17-20 are claims encompassed by the elected Group II. Claim 21 should also be included in Group II as indicated above. Applicants note that each of these claims recites a markush group of markers. It is not clear to Applicants whether the Examiner is requiring an election of a single marker from these claims or an election of one of the markush groups recited in these claims. If the requirement is for the election of a markush group, Applicants provisional elect the species of drusen-associated markers recited in claim 9. If the requirement is for the election of a single marker, Applicants provisionally elect with traverse the species of elastin. Applicants traverse such a requirement because the requirement is not appropriate since many markers in one markush group would be obvious over each other (e.g., different immunoglobulin chains in claim 10).

Preliminary Amendment

Claims 1-67 are pending in the application and subject to restriction and election requirement. With entry of this amendment, claims 8-10, 12, 14, and 16-20, 36, and 67 have been amended. Applicant submits that the claim amendments are made for improved clarity or correction of typographical errors. The amendments are directed to matters of form only and are not intended to affect the scope of any claim. All claim amendments are fully supported by the application. No new matter has been added by the amendments.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400 x 5209.

Respectfully submitted,

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Appendix: Marked-up version of elected claims

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Marked-up Version of All Claims of Group II
(including claim 21 that should be rejoined with Group II)
(claims unamended herewith appear in small font)

1. A method for diagnosing, or determining a predisposition to developing, an arterial wall disruptive disorder in a subject, comprising detecting one or more genotypic or phenotypic markers for macular degeneration in the eye, wherein said marker is indicative of arterial wall disruptive disorder or of a predisposition to developing arterial wall disruptive disorder.

2. The method of claim 1, wherein said arterial wall disruptive disorder is selected from the group consisting of: an aortic aneurysm, a peripheral aneurysm, a visceral aneurysm, and an intracranial aneurysm.

3. The method of claim 1, wherein said arterial wall disruptive disorder is a dissecting aneurysm.

4. The method of claim 2, wherein said aortic aneurysm is an abdominal aortic aneurysm (AAA).

5. The method of claim 2, wherein said aortic aneurysm is a thoracic aortic aneurysm (TAA).

6. The method of claim 1, wherein said macular degeneration is age-related macular degeneration (AMD).

7. The method of claim 1, wherein said macular degeneration is the exudative or neovascular (wet) form, which is characterized by disciform scars and/or choroidal neovascularization (DS/CNV) or an exudative precursor phenotype.

8. (Amended) The method of claim 1, wherein said marker **[includes]** **is** the presence of drusen in the subretinal pigmented epithelial (sub RPE) space.

9. (Amended) The method of claim 1, wherein said marker **[includes]** **is** one or more drusen-associated markers.

10. (Amended) The method of claim 9, wherein said drusen-associated marker is selected from the group consisting of immunoglobulins, amyloid A (α1 amyloid A), amyloid P component, **[C5 and]**C5b-9 terminal complexes, HLA-DR, **[fibrinogen, Factor X, and prothrombin,]** complements 3, 5 and 9, complement reactive protein (CRP), immunoglobulin lambda and kappa light chains, Factor X, HLA-DR, apolipoprotein A,

apolipoprotein E, antichymotrypsin, β2 microglobulin, **[factor X,]** fibrinogen, prothrombin, thrombospondin, elastin, collagen, vitronectin, ICAM-1, LFA1, LFA3, B7, IL-1, IL-6, IL-12, TNF-alpha, GM-CSF, heat shock proteins, colony stimulating factors (GM-CSF, M-CSFs), TNFα, and IL-10.

12. (Amended) The method of claim 9, wherein said drusen-associated marker is a phenotypic marker **[is]** selected from the group consisting of RPE cell death or dysfunction, immune mediated events, dendritic cell proliferation, **dendritic cell** migration, **dendritic cell** differentiation, **dendritic cell** maturation and activation in the sub RPE space, the presence of disciform scars, the presence of choroidal neovascularization**, and [and/or]** the **presence [prescence]** of choroidal fibrosis.

14. (Amended) The method of claim 12, wherein said immune mediated event **[may be] is** detected by detecting an auto-antibody, detecting choroidal dendritic cells, detecting accumulation of leukocytes in the choroid, detecting an increase in HLA-DR immunoreactivity of retinal microglia, detecting an increase in the synthesis of type VI collagen**, or [and]** detecting an up-regulation of an immune-associated molecule.

15. The method of claim 14, wherein said auto-antibody is an antibody directed against drusen, RPE, or a retinal antigen.

16. (Amended) The method of claim 14, wherein said immune-associated molecule **[which]** is selected from the group consisting of immunoglobulins, complement, complement receptors, chemokines, cytokines, CD antigens, MHC antigens, acute phase reactants, proteases, protease inhibitors, immune complexes, and antigens.

17. (Amended) The method of claim 12, wherein dendritic cell maturation and proliferation is detected by detecting GM-CSF, IL-4, IL-3, SCF, FLT-3**, or [and]** TNFα.

18. (Amended) The method of claim 12, wherein said migration and differentiation in the sub RPE space **[may be] is** detected by determining the presence and/or level of **at least one [a]** dendritic cell marker **[or combination of markers is]** selected from the group consisting of CD1a, CD4, CD14, CD68, CD45, CD83, CD86 and S100.

19. (Amended) The method of claim 12, wherein said fibrosis **is** **[in said macula may be]** detected by determining the presence or level of elastin, fragments of elastin, collagen, or fragments of collagen.

20. (Amended) The method of claim 12, wherein said fibrosis **is** **[in said macula may be]** detected by examining the expression of at least one marker selected from the group consisting of elastin, fibrillin-2, PI-1, PI-2, **[b]β**-1 integrin, emilin, fibulins, collagens, ficolin, HME, MMPs, TIMPs, lammin, Big H3, lysyl oxidases, LTLPs, PLOD, vitronectin, MFAP-1 and MFAP-2.

21. The method of claim 9, wherein said drusen-associated marker is a genotypic marker selected from the group consisting of HLA-DR, CD68, vitronectin, apolipoprotein E, clusterin and S-100, heat shock protein 70, death protein, proteasome, Cu/Zn superoxide dismutase, cathepsins, and death adaptor protein RAIDD.

36. (Amended) A method for diagnosing, or detecting a predisposition to developing, an arterial wall disruptive disorder in a subject, comprising performing an immunoassay on a sample obtained from said subject using an antibody specific for a gene product indicative of macular degeneration, wherein detection of the presence of bound antibody indicates that the subject has macular degeneration or a predisposition to developing macular degeneration and therefore has an arterial wall disruptive disorder or a predisposition **[for]** **to** developing an arterial wall disruptive disorder.

37. A kit for diagnosing , or detecting a predisposition to developing, an arterial wall disruptive disorder, comprising reagents for performing the immunoassay of claim 36.

67. (Amended) A kit for diagnosing arterial wall disruptive disorder comprising at least two antibodies selected from the group consisting of**[:]** an anti-elastin antibody, **[and]** **an** anti-collagen antibody, an anti-chemokine antibody, and **an** anti-vitronectin antibody.